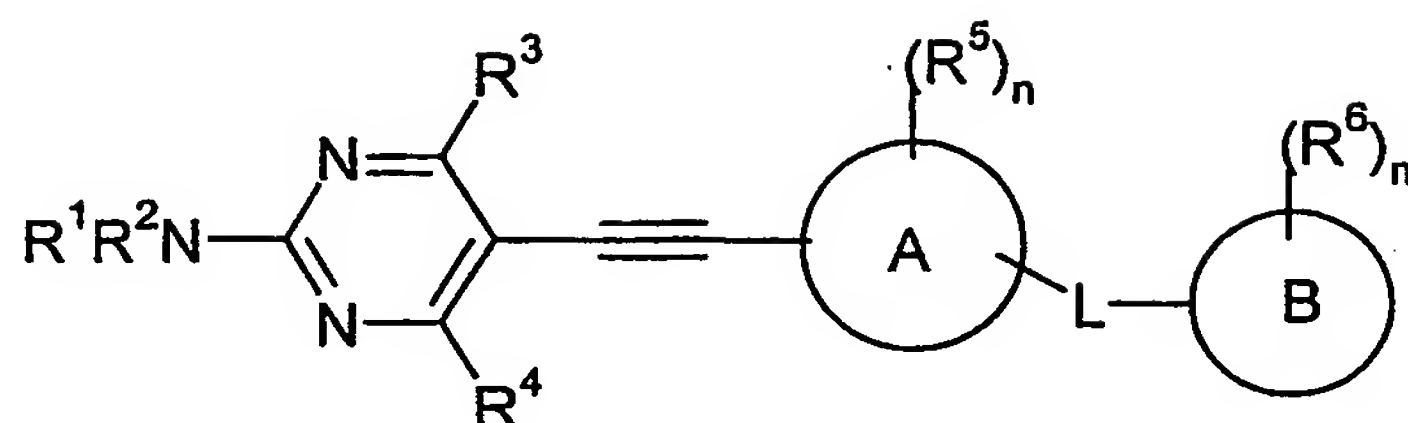


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CLAIMS

1. A compound of the Formula I:



Formula I

wherein:

R¹ and **R²** are independently selected from hydrogen, (1-6C)alkylsulfonyl, phenyl(CH₂)_u- wherein u is 0, 1, 2, 3, 4, 5 or 6, (1-6C)alkanoyl, (1-6C)alkyl, (1-6C)alkoxycarbonyl, (3-6C)cycloalkyl(CH₂)_x- in which x is 0, 1, 2, 3, 4, 5 or 6, or a 5 or 6 membered heteroaryl ring, or **R¹** and **R²** together with the nitrogen atom to which they are attached represent a saturated or partially saturated 3 to 7 membered heterocyclic ring optionally containing another hetero atom selected from N or O;

wherein the (1-6C)alkyl, the (1-6C)alkanoyl and the (3-6C)cycloalkyl groups are

optionally substituted by one or more groups independently selected from

fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy,

(1-6C)alkoxy(1-6C)alkoxy(1-6C)alkoxy, amino, mono(1-6C)alkylamino,

di-[(1-6C)alkyl]amino, carbamoyl, mono(1-6C)alkylcarbamoyl,

di-[(1-6C)alkyl]carbamoyl, -N(R^d)C(O)(1-6C)alkyl in which R^d is hydrogen or

(1-6C)alkyl, a saturated or partially saturated 3 to 7 membered heterocyclic

ring, or a 5 or 6 membered heteroaryl ring,

wherein the (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy and

(1-6C)alkoxy(1-6C)alkoxy(1-6C)alkoxy groups and the (1-6C)alkyl groups of the mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino,

mono(1-6C)alkylcarbamoyl, di-[(1-6C)alkyl]carbamoyl and/or

-N(R^d)C(O)(1-6C)alkyl groups are optionally substituted by one or more hydroxy groups;

wherein the phenyl is optionally substituted by one or more groups independently selected from halo, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, wherein the (1-6C)alkyl and the (1-6C)alkoxy

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groups are optionally substituted by one or more groups independently selected from hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino; and wherein any heterocyclic and heteroaryl rings within R^1 and/or R^2 are optionally independently substituted by one or more of the following:

5 (1-4C)alkyl, (1-4C)alkoxy, (1-4C)alkoxy(1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or $-C(O)(CH_2)_zY$ wherein z is 0, 1, 2 or 3 and Y is selected from hydrogen, hydroxy, (1-4C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino or a saturated or partially

10 saturated 3 to 7 membered heterocyclic ring;

and provided that when R^1 and/or R^2 is a (1C)alkanoyl group, then the (1C)alkanoyl is not substituted by fluoro or hydroxy;

R^3 and R^4 are independently selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy,

15 wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from: fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, carbamoyl, mono(1-6C)alkylcarbamoyl or di-[(1-6C)alkyl]carbamoyl, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6

20 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following:

(1-4C)alkyl, (1-4C)alkoxy, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

25 or one of R^3 and R^4 is as defined above and the other represents a group $-NR^1R^2$ as defined above;

A represents an aryl group or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl,

30 pyrazinyl or 1,3,5-triazinyl;

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R^5 is selected from cyclopropyl, cyano, halo, (1-6C)alkoxy or (1-6C)alkyl, wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by cyano or by one or more fluoro;

5 n is 0, 1, 2 or 3;

10 L is attached meta or para on ring A with respect to the point of attachment of the ethynyl group and represents $-C(R^a R^b)C(O)N(R^9)-$, $-N(R^8)C(O)C(R^a R^b)-$, $-N(R^8)C(O)N(R^9)-$, $-N(R^8)C(O)O-$, or $-OC(O)-N(R^9)-$, wherein R^8 and R^9 independently represent hydrogen or (1-6C)alkyl and wherein R^a and R^b independently represent hydrogen or (1-6C)alkyl or R^a and R^b together with the carbon atom to which they are attached represent (3-6C)cycloalkyl;

15 B represents a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring, an aryl group, a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl, or a 8, 9 or 10 membered bicyclic group which optionally contains 1, 2, 3 or 4 heteroatoms independently
20 selected from N, O and S and which is saturated, partially saturated or aromatic;

R^6 is selected from halo, cyano, oxo, a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring, and $-N(R^c)C(O)(1-6C)alkyl$ in which R^c is hydrogen or (1-6C)alkyl; or

25 R^6 is selected from (1-6C)alkyl, $-S(O)_p-(1-6C)alkyl$ wherein p is 0, 1 or 2, or (1-6C)alkoxy, wherein the (1-6C)alkyl, $-S(O)_p-(1-6C)alkyl$ and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, a (3-7C)cycloalkyl ring or a saturated or partially saturated 3
30 to 7 membered heterocyclic ring; and

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wherein the (3-7C)cycloalkyl ring and saturated or partially saturated 3 to 7 membered heterocyclic ring are optionally independently substituted by one or more groups selected from (1-6C)alkyl; and

5 **m** is 0, 1, 2 or 3;

and when **B** is a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a saturated or partially saturated 8, 9 or 10 membered bicyclic group, the rings and the bicyclic group optionally bear 1 or 2 oxo or thioxo substituents;
10 and salts thereof.

2. A compound of Formula I according to Claim 1, wherein:

15 **R**⁶ is selected from halo, cyano, a (3-7C)cycloalkyl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or an alkanoylamino group
-N(**R**⁶)C(O)(1-6C)alkyl in which **R**⁶ is hydrogen or (1-6C)alkyl; or
R⁶ is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the (1-6C)alkyl and the (1-6C)alkoxy groups are optionally substituted by one or more groups independently selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino,
20 di-[(1-6C)alkyl]amino, a (3-7C)cycloalkyl ring or a saturated or partially saturated 3 to 7 membered heterocyclic ring;
and salts thereof.

3. A compound of the Formula I according to claim 1, wherein:

25 **R**¹ and **R**² are independently selected from hydrogen, (1-6C)alkylsulfonyl, phenyl(CH₂)_u- wherein **u** is 0, 1, 2, 3, 4, 5 or 6, (1-6C)alkanoyl, (1-6C)alkyl, (1-6C)alkoxycarbonyl, or (3-6C)cycloalkyl(CH₂)_x- in which **x** is 0, 1, 2, 3, 4, 5 or 6 or **R**¹ and **R**² together with the nitrogen atom to which they are attached represent a saturated or partially saturated 3 to 7 membered heterocyclic ring optionally
30 containing another hetero atom selected from N or O;

wherein the alkyl and the cycloalkyl groups are optionally substituted by one or more groups selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, a saturated or partially

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5 saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

10 and wherein the phenyl is optionally substituted by one or more groups selected from halo, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, wherein the (1-6C)alkyl or (1-6C)alkoxy are optionally substituted by hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino;

15 R^3 and R^4 are independently selected from hydrogen, (1-6C)alkyl or (1-6C)alkoxy wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups selected from fluoro, hydroxy, (1-6C)alkyl, (1-6C)alkoxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring, wherein said heterocyclic and heteroaryl rings are optionally independently substituted by one or more of the following: (1-4C)alkyl, hydroxy, amino, mono(1-6C)alkylamino or di-[(1-6C)alkyl]amino or a saturated or partially saturated 3 to 7 membered heterocyclic ring;

20 or one of R^3 and R^4 is as defined above and the other represents a group $-NR^1R^2$ as defined above;

25 R^5 is selected from cyano, halo, (1-6C)alkoxy or (1-6C)alkyl optionally substituted by cyano or by one or more fluoro;

30 **B** represents a (3-7C)cycloalkyl ring, an aryl or a 5 or 6 membered heteroaryl ring selected from furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl or 1,3,5-triazinyl;

R^6 is selected from halo, cyano, a saturated or partially saturated 3 to 7 membered heterocyclic ring or an alkanoylamino group $-N(R^c)C(O)(1-6C)alkyl$ in which R^c is

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hydrogen or (1-6C)alkyl; or R^6 is selected from (1-6C)alkyl or (1-6C)alkoxy, wherein the alkyl and the alkoxy groups are optionally substituted by one or more groups selected from cyano, fluoro, hydroxy, (1-6C)alkoxy, amino, mono(1-6C)alkylamino, di-[(1-6C)alkyl]amino, or a saturated or partially saturated
5 3 to 7 membered heterocyclic ring; and

m is 0, 1, 2 or 3; and when m is at least 2 then two substituents on adjacent carbon atoms in ring B may together represent a methylenedioxy group;

10 and wherein A, L and n are as defined in Claim 1.
and salts thereof.

4. A compound according to any one of Claims 1, 2 and 3 wherein A is selected from phenyl, pyridyl, thiazolyl, thiadiazolyl or pyrimidinyl.

15

5. A compound accordingly to any one of the preceding claims wherein B is selected from phenyl, 2,3-di-hydro-indenyl, piperidinyl, pyridyl, pyrazolyl, isothiazolyl, thiadiazolyl, isoxazolyl, benzodioxinyl, benzodioxolyl or tetrahydropyranyl

20 6. A compound accordingly to any one of the preceding claims wherein L is selected from $-N(R^8)C(O)N(R^9)-$, $-N(R^8)C(O)O-$ or $-N(R^8)C(O)CH_2-$ wherein R^8 and R^9 independently represent hydrogen or (1-6C)alkyl.

25 7. A compound accordingly to any one of the preceding claims wherein R^1 and R^2 are both hydrogen or R^1 is hydrogen or (1-6C)alkyl and R^2 is (1-6C)alkyl

wherein (1-6Calkyl) is optionally substituted by hydroxy, amino, mono(1-6C)alkylamino or di(1-6C)alkylamino, carbamoyl, (1-6C)alkoxy, (1-6C)alkoxy(1-6C)alkoxy, $-N(R^d)C(O)(1-6C)alkyl$ in which R^d is hydrogen or (1-6C)alkyl, aryl (particularly phenyl), a saturated or partially saturated 3 to 7
30 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring;
wherein the (1-6C)alkoxy, mono(1-6C)alkylamino and $-N(R^d)C(O)(1-6C)alkyl$ groups are optionally substituted by hydroxy;

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wherein an aryl ring, a saturated or partially saturated 3 to 7 membered heterocyclic ring or a 5 or 6 membered heteroaryl ring is optionally substituted by (1-4C)alkyl, (1-4C)alkoxy or -C(O)CH₂Y wherein Y is selected from hydroxy or di(1-6C)alkylamino.

5

8. A compound accordingly to any one of the preceding claims wherein R³ and R⁴ are both hydrogen.

9. A compound accordingly to any one of the preceding claims wherein R⁶ is independently selected from halo, cyano, oxo, (3-7C)cycloalkyl, a saturated 3 to 7 membered heterocyclic ring (optionally substituted by (1-4C)alkyl), -N(R^c)C(O)(1-6C)alkyl wherein R^c is hydrogen or (1-6C)alkyl (particularly (1-4C)alkyl), (1-6C)alkyl (optionally substituted by up to three groups independently selected from halo) or (1-6C)alkoxy and m is selected from 1 or 2.

15

10. A compound according to Claim 1 which is any one or more of examples 1 to 152 or a salt thereof.

11. A pharmaceutical composition which comprises a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10 in association with a pharmaceutically acceptable diluent or carrier.

12. A compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10, for use as a medicament.

25

13. Use of a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10, in the manufacture of a medicament for use as a Tie2 receptor tyrosine kinase inhibitor in a warm-blooded animal such as man.

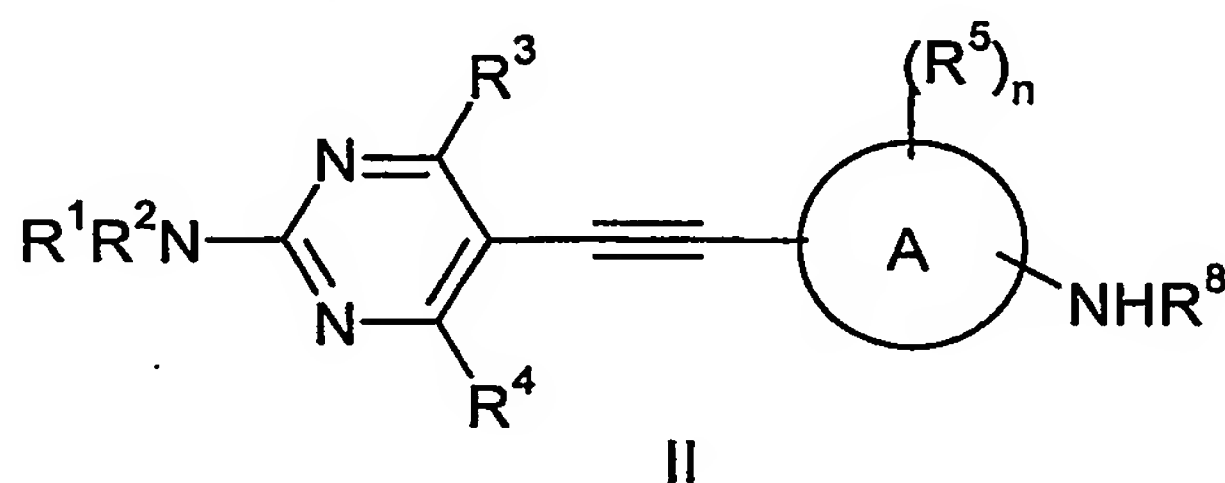
14. Use of a compound of the Formula I, or a pharmaceutically acceptable salt thereof, as defined in claims 1 to 10, in the manufacture of a medicament for use in the production of an anti-angiogenic effect in a warm-blooded animal such as man.

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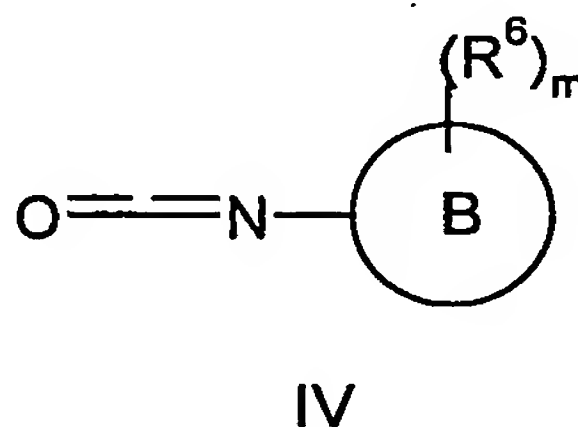
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15. A process for preparing a compound of formula I, or salt thereof, as defined in Claim 1, or a pharmaceutically acceptable salt thereof (wherein $R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}$, L, ring A and ring B, n and m are, unless otherwise specified, as defined in Claim 1) comprising:

- 5 (a) For compounds of the formula I wherein L is $-N(R^8)C(O)N(H)-$, the reaction of a compound of the formula II:

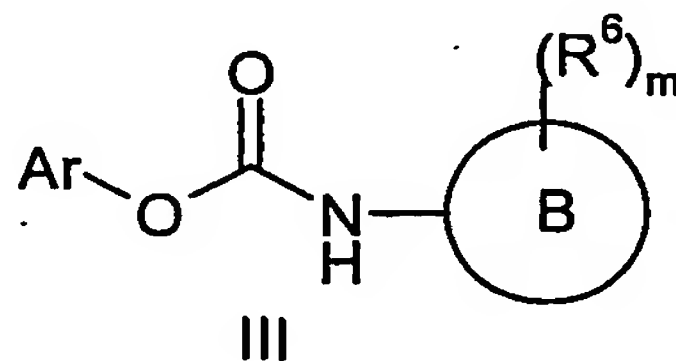


wherein $R^1, R^2, R^3, R^4, R^5, R^8, n$ and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an isocyanate of the formula IV:



wherein R^6, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

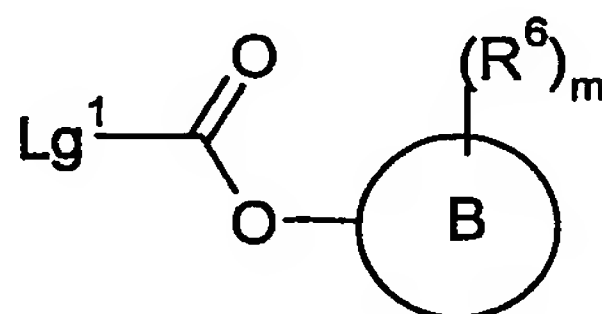
- 15 (b) For compounds of the formula I wherein L is $-N(R^8)C(O)N(H)-$, the reaction of a compound of the formula II as defined above with an aryl carbamate of the formula III:



wherein Ar is a suitable aryl group, for example phenyl, and R^6, m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

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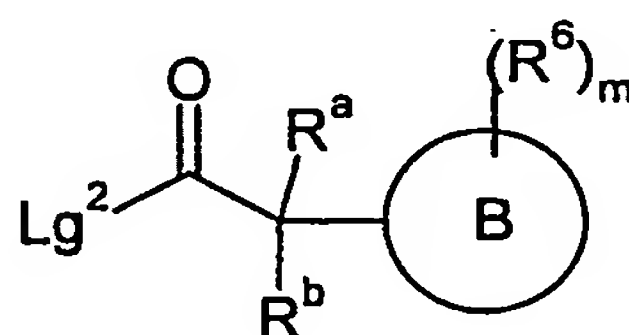
- (c) For compounds of the formula I wherein L is $N(R^8)C(O)-O-$, the reaction of a compound of the formula II as defined above with a compound of the formula XI:



XI

5 wherein Lg^1 is a suitable displaceable group for example halogeno (such as fluoro, chloro or bromo) and R^6 , m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

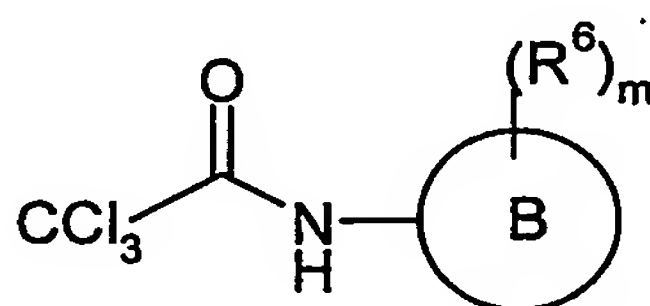
- (d) For compounds of the formula I wherein L is $N(R^8)C(O)C(R^aR^b)$, the reaction of a compound of the formula II as defined above with a compound of the formula IX:



IX

10 wherein Lg^2 is a suitable displaceable group for example hydroxy, halogeno (such as fluoro, chloro or bromo), $R^x-C(O)-O-$ or R^x-O- (wherein R^x is a suitable alkyl or aryl group) and R^6 , R^a , R^b , m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

- 15 (e) For compounds of the formula I wherein L is $-N(R^8)C(O)N(H)-$, the reaction of a compound of the formula II as defined above with a trichloroacetylamine of the formula XIII:

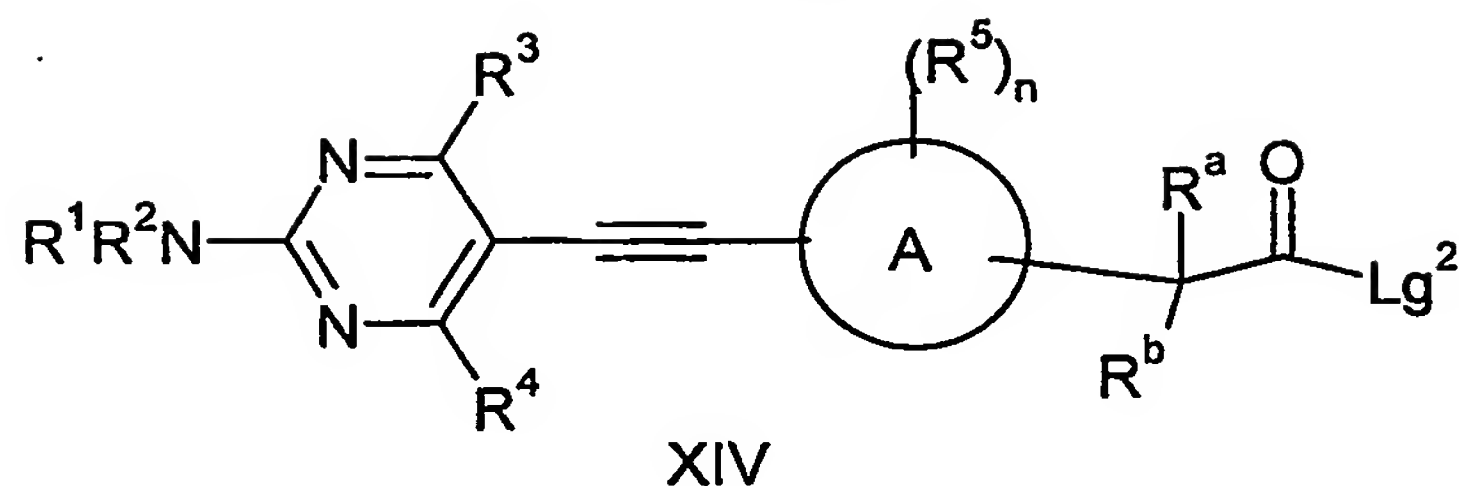


XIII

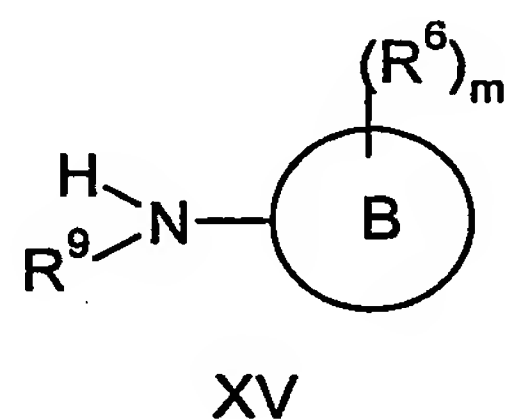
wherein R^6 , m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

- 20 (f) For compounds of the formula I wherein L is $-C(R^aR^b)C(O)N(R^9)-$, the reaction of a compound of the formula XIV:

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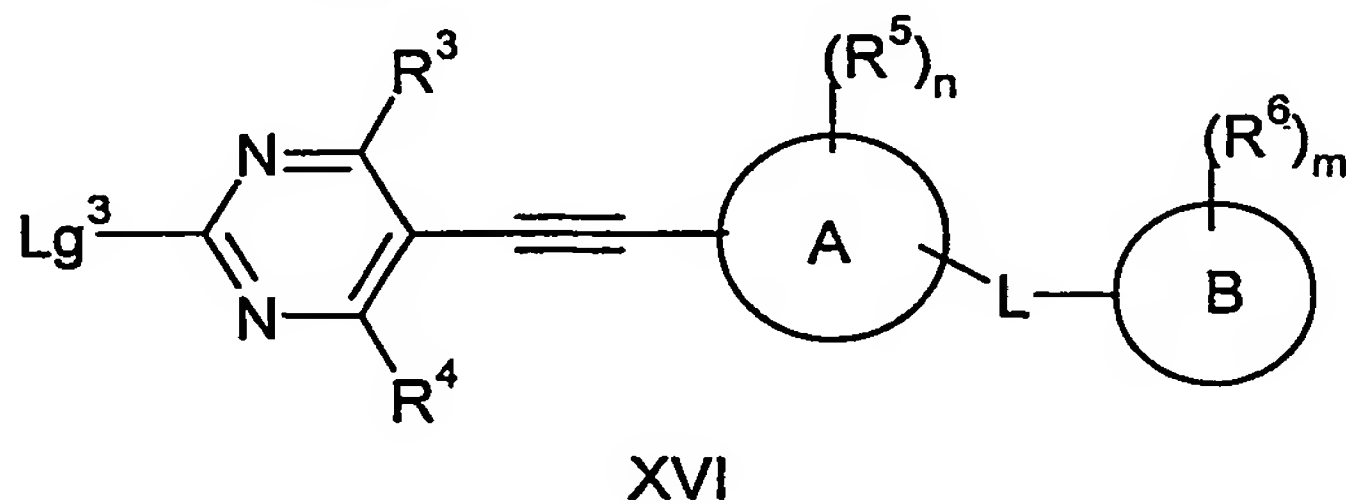
wherein Lg^2 is a suitable displaceable group as described above and R^1 , R^2 , R^3 , R^4 , R^5 , R^a , R^b , n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV:



5

wherein R^6 , R^9 , m and B have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

(g) The reaction of a compound of the formula XVI:

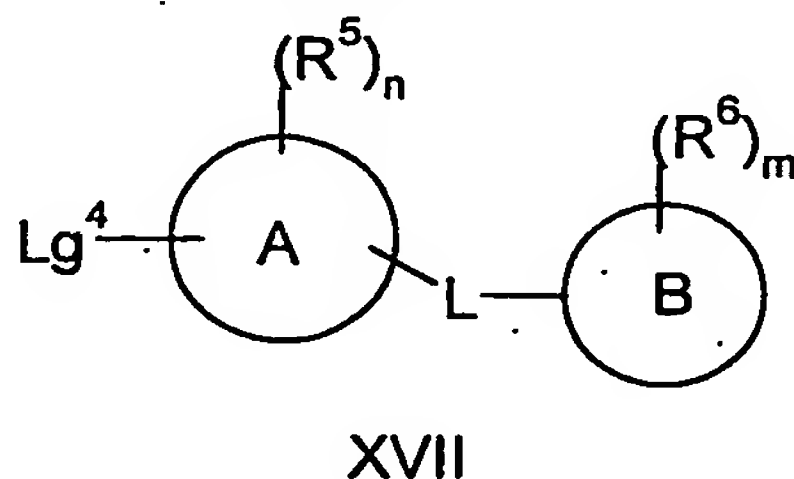


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wherein Lg^3 is a suitable displaceable group for example halogeno (such as fluoro, chloro, bromo or iodo), methyl sulfonyl, methylthio or aryloxy (such as phenoxy) and R^3 , R^4 , R^5 , R^6 , n , m , A , B and L have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula HNR^1R^2 , wherein R^1 and R^2 have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

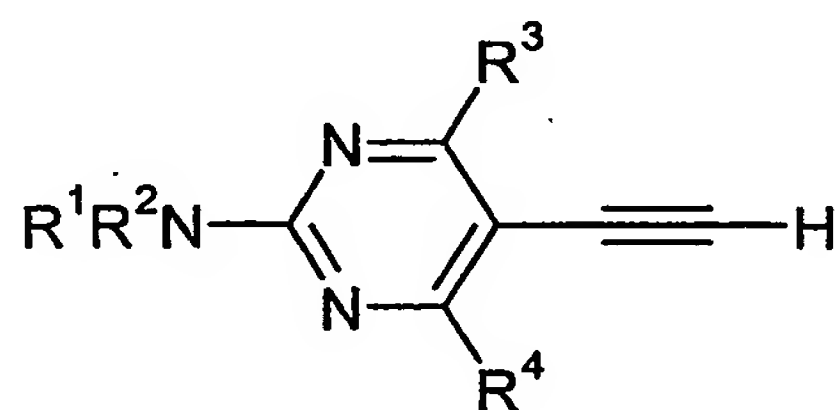
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(h) The reaction of a compound of the formula XVII:



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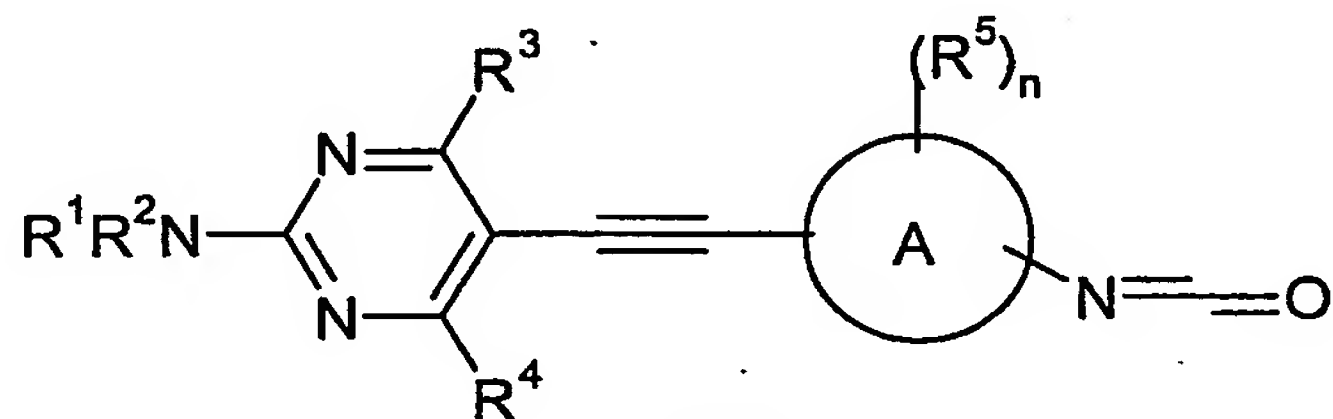
wherein Lg^4 is a suitable displaceable group for example halogeno (such as chloro, bromo or iodo) or a sulfonyloxy group (such as trifluoromethylsulfonyloxy) and R^5 , R^6 , n , m , A , B and L have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an alkyne of the formula XVIII:



XVIII

wherein R^1 , R^2 , R^3 and R^4 have any of the meanings defined hereinbefore except that any functional group is protected if necessary; or

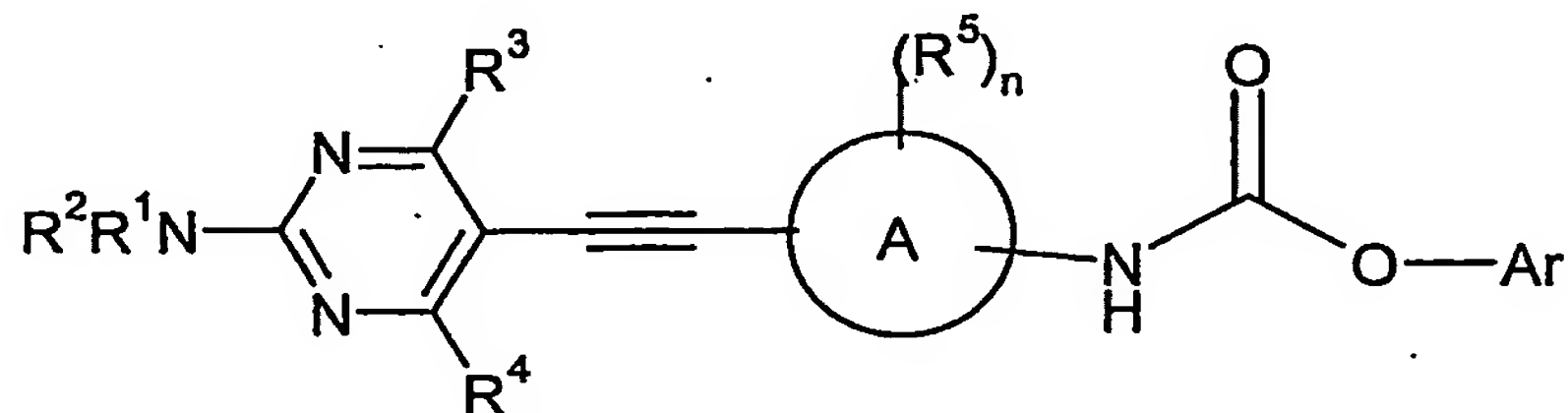
- (i) For compounds of the formula I wherein L is $-N(H)C(O)N(R^9)-$, the reaction of an isocyanate of the formula XIX:



XIX

wherein R^1 , R^2 , R^3 , R^4 , R^5 , n and A have any of the meanings defined hereinbefore except that any functional group is protected if necessary, with an amine of the formula XV as defined above; or

- (j) For compounds of the formula I wherein L is $-N(H)C(O)N(R^9)-$, the reaction of a compound of the formula XX:



XX

wherein Ar is a suitable aryl group, for example phenyl, and R^1 , R^2 , R^3 , R^4 , R^5 , n and A have any of the meanings defined hereinbefore except that any functional

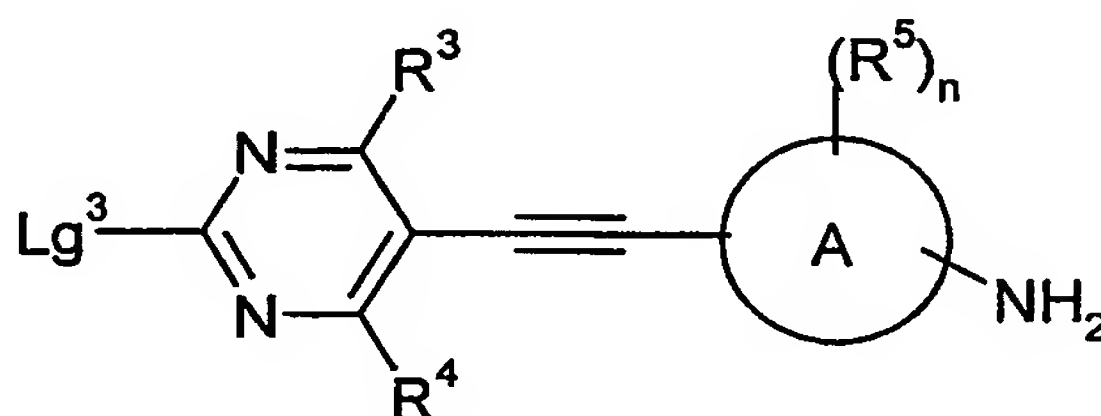
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group is protected if necessary, with an amine of the formula XV as defined above.

and thereafter if necessary:

- 5 i) converting a compound of the Formula (I) into another compound of the Formula (I);
 ii) removing any protecting groups;
 iii) forming a salt.

16. A compound selected from Formulae II, XIV, XVI, XIX and XX as defined in Claim 15 or a compound of Formula VIc:



VIc

10

or salt thereof, wherein Lg^3 , R^3 , R^4 , R^5 and n are as defined in Claim 15.